Correlated time-lapse imaging and single cell molecular analysis of human embryo development

Grant Award Details

Correlated time-lapse imaging and single cell molecular analysis of human embryo development

Grant Type: Basic Biology III

Grant Number: RB3-02209

Project Objective: Time-lapse imaging and single cell analysis will be used to elucidate quality and viability indices of pre-implantation stage human embryos. Information then used to improve development of gold standard pluripotent stem cell lines, including iPSC.

Investigator:

Name:	Aaron Hsueh
Institution:	Stanford University
Type:	PI

Disease Focus: Fertility

Human Stem Cell Use: Embryonic Stem Cell, iPS Cell

Cell Line Generation: Embryonic Stem Cell, iPS Cell

Award Value: $1,259,733

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Grant Application Details

Application Title: Correlated time-lapse imaging and single cell molecular analysis of human embryo development

Public Abstract: We understand little about human development especially at the earliest stages. Yet human developmental biology is very important to stem cell biology and regenerative medicine for two reasons: 1) Understanding human developmental pathways especially of embryonic differentiation will inform our efforts to derive pluripotent stem cells and differentiate them to stable progenitors that are suitable for transplantation or pharmaceutical applications. Clearly, human development follows well-defined pathways that we are just beginning to elucidate. 2) Understanding human development will allow us to translate findings to the clinic to alleviate common problems of women's and children's health. Errors in the earliest stages of development are the most common cause of all birth defects in the human population and yet we know little of the fundamental ways in which errors occur. Our lack of knowledge is likely enhanced by the complete ban of federal funding for this research in spite of the fact that each year there is increased clinical use of procedures such as IVF.

Thus, here we seek to build a map of human development that combines imaging (microscopic) data, molecular data, genetic and epigenetic data to describe human pluripotent blastomeres (cells) and their potentials. We note that events in the first few cell divisions, even before human embryos turn on their own genes, have repercussions to later generations of cells and the overall health and welfare of the embryo and fetus (and likely adult).

Our goals are based on our research over several years in which we initiated construction of a map of pathways and programs that function during embryo development. Our studies provide methods and algorithms for early diagnosis of embryo potential in clinics and should be extended to the diagnosis of the general health of pluripotent stem cell populations. We expect that via translation of our basic studies to the clinic, we will improve outcomes of IVF in terms of birth of healthy offspring and decrease devastating and common adverse outcomes such as multiple births with attending complications to organ development, epigenetic errors that may result in miscarriage, and need to reduce fetal number to increase odds of survival of siblings and/or mother. Thus, this research may yield benefits to both maternal/fetal health and stem cell biology and regenerative medicine.

Statement of Benefit to California: Stem cell biology and regenerative medicine holds great promise for the citizens of California in terms of establishing a superior basic science infrastructure, translating findings to the clinic for improved health and designing new diagnostics to prevent disease and allow screening of new pharmaceutical agents. There are many promising applications with pluripotent human embryonic stem cells (hESCs) and clinical trials are beginning in several biomedical applications. Yet, we lack an understanding of fundamentals of human biology, especially of the earliest stages. Indeed, we know remarkably little about the relationship of human embryonic cells (blastomeres in the preimplantation embryo), hESCs and induced pluripotent stem cells. This lack of knowledge is costly to the health of Californians today and in the future. First, we have numerous practices in the reproductive arena that carry a substantial burden in terms of diverse adverse outcomes that include prenatal birth and associated risks, increased risk of epigenetic/genetic errors in development, and a need to balance the safety of carrying a multiple-pregnancy with the health of the mother. It is clear that we can improve the health of women and children through knowledge of human embryo development, even though federal funding is not allowed in this arena. Moreover, we can provide increased knowledge of the legitimacy (relationship to nature) of stem cell lines that we derive and thus employ natural programs to improve pluripotent stem cell lines. Successful completion of this research will lead to clinical applications and positively impact a relatively-large segment of the California population.

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